Remarks

The Office Action mailed 26 August 2004 has been received and reviewed.

The specification has been amended to clarify the benefit claim under 35 U.S.C. §119(e).

Claims 1, 19, 26, 40, and 53 having been amended, claims 56-58 having been added, and claims 24 and 29 having been canceled, the pending claims are claims 1-12, 19-23, 25-28, 33-38, 53, and 56-58. Support for the claim amendments is found throughout the specification.

Reconsideration and withdrawal of the rejections are respectfully requested.

The 35 U.S.C. §112, Second Paragraph, Rejection

The Examiner rejected claims 1-12, 19-29, 33-38, 40-43 and 53 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. This rejection is respectfully traversed.

A patent claim is sufficiently definite to satisfy 35 U.S.C. § 112, second paragraph, if one skilled in the art would understand the bounds of the claim when read in light of the specification. Exxon Research v. United States, 60 USPQ2d 1272 (Fed. Cir. 2001) (citing Miles Labs., Inc. v. Shandon, Inc., 27 USPQ2d 1123, 1126 (Fed. Cir. 1993). The Examiner asserts that claims 1-12, 19-29, 40-43, and 53 fail to satisfy 35 U.S.C. § 112, second paragraph, because they do not provide sufficient structural and functional limitations to enable the skilled artisan to ascertain the metes and bounds of the claimed invention, as well as failing to provide a functional nexus for the four nucleotide sequences.

Applicants have amended claims 1, 19, 26, 40, and 53 to clarify the functional nexus between the structural and functional limitations of the claims. In particular, the claims have been amended to be directed to pseudotyped-retrovirus-producing eukaryotic cells, or related aspects of the invention. Pseudotyped retroviruses are described in the specification as retroviruses provided with different envelope glycoproteins to expand the host range of the

retrovirus (see page 2, lines 4-12); this function is clear from recitation of the term "pseudotyped" in the claims. Structures that form the pseudotyped retrovirus in the context of a eukaryotic cell include the proteins encoded by the retroviral nucleotide sequences (namely, Gag, Pro, and Pol), which are distinctive for retrovirus formation, and sequences that form the viral glycoproteins, providing the "pseudotyped" aspect of the retrovirus, expanding or altering host range. These structures are recited in the claims. A functional nexus between the presence of these nucleotide sequence structures and the altered or expanded host range of a pseudotyped retrovirus that result from expression of these sequences is thus present, and would be clear to workers skilled in the art.

The Examiner also questioned the sufficiency of the detail provided regarding the arrangement of the nucleotide sequences on expression vectors. The Examiner is directed to page 17 line 4 to page 18, line 2, which describes various arrangements of the nucleotide sequences on expression vectors. Applicants have also provided new dependent claims 56 - 58 directed to several preferred arrangements. Applicants note, however, that workers skilled in the art realize that the nucleotide sequences can be delivered and function independently, or in any combination, relative to each other, and that exact arrangement of the sequences on the expression vectors does not significantly impinge on the structural/functional nexus of the invention, as described above.

On a related note, the Examiner stated that the transfected constructs may result in transient or stable expression of the proteins. Applicant replies that both transient and stable expression of retroviral particles are within the scope of the independent claims. Both types of expression are disclosed within the specification, and examples are provided that demonstrate how both types of expression may be accomplished (see, for example, Example 2 and Example 3 for transient and stable expression, respectively, using RRV). Inclusion of both types of expression does not render the claims vague and indefinite. Dependent claims to cells having chromosomally integrated nucleotide sequences are provided that are directed specifically to stable cell lines.

The Examiner further rejected claims 19-29 as vague and indefinite for being based on an "illogical" preamble. Applicants have amended claims 19, 26, and 53 to clarify that a cell is not formed; rather, a cell is modified to prepare a pseudotyped-retrovirus-producing cell. If these amendments have not obviated the rejection, Applicants respectfully request that the Examiner provide further clarification on how the preamble is illogical.

The Examiner also rejected claims 40-43 based on use of the phrase "selected ribonucleotide sequence" as vague and indefinite. Applicants have provided guidance as to the identity of selected nucleotide sequences in the specification; for example, on page 15, lines 17-26 or on page 21, line 15 to page 22, line 3. One example of a selected nucleotide sequence discussed in the specification is a sequence producing a marker protein. However, the precise identity and/or function of the selected nucleotide sequence is not crucial to the independent claims of the present application, as they simply refer to a particular nucleotide sequence that is being delivered by the pseudotyped retroviral vector. The claims are not intended to be limited to any particular nucleotide sequence, and there is nothing in the specification that would suggest that any one sequence is preferred over any other. This nucleotide sequence is essentially a passenger of the viral vector, and need not be characterized in any detail to satisfy § 112, second paragraph, as any sequence selected by the user of the invention may be delivered.

The 35 U.S.C. §112, First Paragraph, Rejection

The Examiner rejected claims 1-12, 19-29, 33-38, 40-43, and 53 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner has raised the issue whether adequate support is provided for the broadly claimed genus of RVVPs, producer cell lines, and methods of making said cell lines. This rejection is respectfully traversed.

Note that applicants are assuming the acronym RVVP represents retroviral vector particles, as applicant's specification does not make use of this term, and we would appreciate clarification if our assumption is in error.

The Examiner states that the written description requirement may be satisfied through the disclosure of function and minimal structure when there is a well-established correlation between structure and function. The structures of numerous Gag, Pro, and Pol encoding sequences are well known, and there is a well-established correlation between these structures and the formation of retroviruses. See, for example, Retroviruses, J.M. Coffin, S. H. Hughes, H.E. Varmus, eds., Ch. 1, which states:

> "All retroviruses contain three major coding domains with information for virion proteins: *gag*, which directs the synthesis of internal virion proteins that form the matrix, the capsid, and the nucleoprotein structures; *pol*, which contains the information for the reverse transcriptase and integrase enzymes; and *env*, from which are derived the surface and transmembrane components of the viral envelope protein. An additional, smaller, coding domain present in all retroviruses is *pro*, which encodes the virion protease."

Further, as noted on p. 10, lines 15-30 of the specification, a wide variety of retroviral nucleotide sequences may be used within the scope of the present invention, a number of which are specifically disclosed. The correlation between the structure (foreign viral envelope glycoproteins) and function (expanded host range of a pseudotyped virus) is also well-established, as evidenced by the well-established use of the term "pseudotyped virus" by those skilled in the art. See for example U.S. Patent 5,512,421, issued to Burns et al., provided by applicants in the earlier filed information disclosure statement. As the present application discloses a functional nexus in which the correlation between structure and function is well-established, the burden of providing detailed structural information is reduced. Applicants have, in fact, more than met this reduced burden by providing significant structural data, in the form of numerous examples and the nucleotide sequences encoding for three different viral envelope glycoproteins. Applicants have thus shown possession of the claimed invention.

Applicants acknowledge Examiner's statement that a skilled artisan would reasonably conclude that applicants were "in possession of a recombinant MoMLV expression system that was capable of producing RRV-pseudotyped RVVPs". However, limiting the invention to a single recombinant retroviral vector system (MoMLV) when a wide variety of retroviral vectors are known in the art, as disclosed in the present application, is not be necessary, particularly as applicants are not claiming such retroviral vectors, but rather simply using them as a means to prepare a retrovirus-producing cell. See, for example, page 11, first paragraph, for reference to retroviruses available from the American Type Culture Collection. The only retroviral vector being claimed is the actual pseudotyped retrovirus prepared by the modified eukaryotic cells (see claim 33 and its dependent claims). Furthermore, limiting the invention to Ross River Virus envelope glycoproteins is also unwarranted, as three envelope glycoprotein-encoding nucleotide sequences (Ross River, Ebola, and Marburg) have been specifically disclosed, and the suitability of a wide variety of other viral glycoproteins has also been disclosed. See for example page 12, lines 21 to page 13, line 10, which discloses the suitability of viral glycoproteins from Togaviridae, Paramycoviridae, and Buyaviridae. Given the requirement that the Examiner has the initial burden of presenting, by a preponderance of the evidence, why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims (In re Wertheim, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976)), applicant requests that the rejection under 35 U.S.C. §112, first paragraph should be withdrawn in light of the amendments and the arguments provided above.

Summary

It is respectfully submitted that the pending claims 1-12, 19-23, 25-28, 33-38, 53, and 56-58 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
Purdue Research Foundation

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CERTIFICATE UNDER 37 CFR §1.8:
The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Mail Stop Amendment, Commissioner for Patents, Attn: Examiner Parkin, P.O. Box 1450, Alexandria, VA 22313-1450, on this 17 day of November, 2004, at 11:50 A.M. (Central Time).

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